Incorporation of antimicrobial agents in denture base resin: A systematic review

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SYSTEMATIC REVIEW

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ABSTRACT

Statement of problem. Denture base resins (DBRs), such as polymethyl methacrylate (PMMA), are commonly used in the fabrication of removable dentures because of their physical, mechanical, and esthetic properties. However, the denture base acts as a substrate for microorganism adherence and biofilm formation, which may lead to denture stomatitis and be further complicated by fungal infections, of especial importance with geriatric and immunosuppressed patients. Therefore, methods to enhance the antimicrobial property of DBRs will be beneficial.

Purpose. The purpose of this systematic review was to evaluate the literature on the antimicrobial activity of DBRs incorporating antimicrobial agents or materials.

Material and methods. A search of English peer-reviewed literature up to February 2019 reporting on antimicrobial activity of DBRs with respect to antimicrobial agents or materials, antimicrobial test effects and methods, and conclusion or knowledge gaps was conducted by using Embase, Google Scholar, PubMed, and Web of Science databases. Search terms included denture base resin and antibacterial, denture base resin and antifungal, and denture base resin and antimicrobial. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were applied for subsequent data analysis.

Results. Of 2536 identified articles, 28 met the inclusion criteria for the systematic review. Antimicrobial materials were divided into 3 groups: antimicrobial monomer or copolymer,

phytochemical or phytomedical components, and other compounds. Strategies on how to incorporate these substances into DBRs and their impact on the reduction and prevention of the growth of microorganisms were identified.

Conclusions. Although many efforts have been made to improve the antimicrobial ability of DBRs, this systematic review found that the effectiveness of incorporating of antimicrobial agents into DBRs has not been demonstrated conclusively.

CLINICAL IMPLICATIONS

Potential antimicrobial activity of denture base resins (DBRs) is an important issue for geriatric and immunocompromised patients, and further research is needed to identify techniques of incorporating biodegradable microcapsules or nanocarriers containing organic antimicrobial agents into denture base materials.

INTRODUCTION

Acrylic polymers such as polymethyl methacrylate (PMMA) are the most frequently used materials in the fabrication of removable dental prostheses and have been clinically accepted for over 70 years because of their physical, mechanical, and esthetic properties, as well as low cost, straightforward fabrication, and biocompatibility.[1-5] Interconnected factors such as saliva, levels of acidity (pH), oral microorganisms,[6] and the type of oral prosthesis can generate conditions that may impair natural saliva flow, exert mechanical compression, increase temperature, and decrease light to mucosal tissues.[7] These conditions may influence the accumulation of a denture biofilm and promote cariogenic or periodontal biofilms.[8] A biofilm is a multifaceted consortium of microorganisms that displays a varied range of physical, metabolic, and molecular interactions

among the species within based on its attachment, growth, and survival in the oral cavity.[9] The denture base may act as a reservoir for bacterial species, increasing the likelihood of dental caries and stomatitis and further complicating fungal infection such as by *Candida albicans* (*C. albicans*).[10,11]

C. albicans is the most commonly occurring saprophytic microorganism in a healthy oral cavity, but microbial imbalance caused by the environmental change of being under a denture base may lead to the formation of mucosal inflammatory lesions. These lesions may cause periodontal diseases, oral and gastrointestinal infections, and even death.[11-13] *Candida* associated denture stomatitis (CADS) is identified as a noninflammatory reaction of denture bearing mucosa tissue, commonly caused by the antigens, toxins, and enzymes produced by biofilm microorganisms on DBR surfaces.[14] Denture biofilm can also be related to systemic diseases such as aspiration pneumonia, infectious endocarditis, and pulmonary candidiasis, particularly for long-time denture users or immunocompromised patients.[10,15] The intaglio surface of a maxillary denture acts as an active reservoir for microorganisms with attachment on the palatal mucosal tissue, providing an environment in colonization and pathogenesis.[6] Although the mechanism by which *Candida* adheres to DBR surfaces is not yet fully identified, interaction between hydrophobic or electrostatic bonds, salivary pellicles, and surface roughness have been proposed as a possible method.[16]

Newly fabricated DBR surfaces in the oral cavity can lead to biofilm formation for Gram-positive *streptococci,* rods, Gram-negative bacteria, *Staphylococcus aureus*, and yeast type fungal colonies.[17] The initial adhesion of commensal yeast cells of the genus *Candida* on dentures results in complex fungal biofilm formation, which displays 3 forms of growth: hyphae, pseudohyphae, and blastoconidia, each having its distinctive morphology.[18,19]

During mastication, bacterial or fungal cells may be rinsed by saliva and swallowed. However, biofilms are hard to eliminate, not only because of their strong adhesion to biomaterials but also their penetration of microporosities into the DBR. They often reoccur after discontinuation of drug therapy.[17,20-23] The presence of extracellular matrices around certain microorganisms acts as a protective mechanism, resulting in antimicrobial resilence.[24] Therefore, conventional cleaning methods such as mechanical brushing[25] are not sufficient to remove biofilm from DBR surfaces,[5,24] and treatment for CADS is challenging given the high rate of drug administration required.[22]

Investigations into methods of decreasing biofilm formation by incorporating various antimicrobial materials into the denture base material have been conducted,[8,26] including antimicrobial agents and drugs, antimicrobial copolymers, surface modification via polymeric surface coatings, and fillers.[3,8,15,21,26-29,38-39] However, the authors are unaware of systematic reviews on the effectiveness of these antimicrobial agents and their methods of incorporation and testing. Thus, this systematic review investigated the effect of incorporating organic antimicrobial agents into DBRs.

MATERIAL AND METHODS

An electronic search of the literature was carried out using 4 database systems: Embase, Google Scholar, PubMed, and Web of Science using 3 search terms ‘denture base resin and antibacterial,’ ‘denture base resin and antifungal,’ and ‘denture base resin and antimicrobial.’ The search included all articles reporting antimicrobial activities of DBRs published in English up to and including February 2019.

A total of 4180 published articles and abstracts were identified using the search criteria. Google Scholar identified 1250, 934, and 1260 references respectively that included at least one of the search terms, but, after reading the titles, only 600 articles were relevant to the review. The total number of articles reviewed was 2536 (Table 1).

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used for the data analysis process (Fig. 1). Initially duplicate papers (n=1515) were excluded, and then a further 875 papers were removed by screening for the following terms in the titles which, although related, did not address incorporation of antimicrobials into DBRs; for example, coating or surface treatment, composite resins, denture cleaning or disinfectant or sterilization methods, flexible denture bases, physical or mechanical property test, and silicone soft lining materials. Papers with incomplete information, review and update articles, theses, and websites were also removed. One hundred and forty-six potentially relevant articles were subsequently accessed for reading of the full text. After applying the previous exclusion criteria, another 80 records were removed. Finally, 15 hand-searched articles were also included, resulting in a total of 81 papers for the systematic review.

RESULTS

Of the 81 papers identified in the literature search, 28 examined the incorporation of organic agents (the remaining were inorganic)[50] and were the subject of this review (Supplementary Table 1). The column headings in Supplementary Table 1 are based on the incorporated antimicrobial materials or agents, antimicrobial effects and methods, and conclusion or knowledge gaps. The data from the relevant 28 papers were divided into 3 subgroups:

antimicrobial monomer or copolymer, phytochemical or phytomedical components, and other compounds based on 20 distinguishable materials (Table 2).

DISCUSSION

The purpose of this systematic review was to examine DBRs incorporating organic antimicrobial materials or agents, their antimicrobial effects, and test methods. PMMA polymers are commonly used in denture base fabrication because of their straightforward processing with inexpensive techniques, esthetically pleasing appearance, and high biocompatibility. However, the formation of *C. albicans* dominated biofilms and other pathogens leading to CADS on PMMA DBRs is of concern.[4,49] Investigations have attempted to reduce biofilm formation by incorporating various materials into PMMA.[8] The following organic compounds identified in the systematic review as potential antimicrobial agents will be explored in relation to their ability to be used with dental materials.

Antimicrobial monomer or copolymer

Methacrylic acid (MAA) is a colorless, liquid, and carboxylic acid organic compound.[6,51,52] The carboxylate anionic PMMA surface has been shown to improve adsorption of salivary histatin 5 and to have an inhibitory effect on *C. albicans* adhesion.[44,49] By introducing MAA (anionic monomer) into PMMA, the reaction can create a negative charge on the DBR surface.[6,16,52,53] As denture stomatitis may result from attraction energies between negatively charged *C. albicans* and positively charged DBR,[39] a negatively charged denture surface introduces an anionic repulsive interaction between the PMMA DBR surface and *C. albicans* which contributes to the inhibition of adherence (Fig. 2).[49,52] Another theory is that an increase in the anionic surface charge on PMMA decreases the surface contact angle, creating hydrophobic conditions and

reducing the amount of adherence of *C. albicans*.[49,52,54] However, there is a contrasting view that the incorporation of MAA into DBR may result in a hydrophilic surface with considerable decline of *C. albicans* adhesion.[6,55] 2-hydroxyethyl methacrylate (HEMA), which is based on MAA, is used to fabricate dental adhesive, composite resins,[39] fillers, copolymers, and antimicrobials.[8] Modification of PMMA by adding 15% phosphoric acid 2-hydroxyethyl methacrylate ester (PA2HEME) monomer produced a free hydroxyl unit which established a negative charge at physiological pH,[36] and PA2HEME-PMMA might be used as a therapeutic way to inhibit *C. albicans* adhesion and prevent denture stomatitis.[39] 2-hydroxypropyl methacrylate (HPMA) is also a neutral hydroxyl-rich monomer with OH^- functional groups that alters the biomaterial surface, resulting in decreased protein adsorption and microbial adherence.[63]

Quaternary ammonium salts (QAS) are well-established antiseptics or antimicrobial agents because of their inherent detergent and anti-adhesive properties against a wide range of pathogen microorganisms such as Gram-positive or Gram-negative bacteria, fungi, and particular kinds of viruses.[36,43] Incorporating QAS into MMA to form a quaternary ammonium methacrylate (QAM) maintained its antibacterial activity without sacrificing the mechanical properties of DBR.[36,43,56] Chen et al[29] indicated that when negatively charged bacteria cells contact the highly positively charged quaternary amine (N^+) of a QAS, there is an electrical imbalance that disrupts the cell wall, producing cytoplasmic leakage and cell lysis.[15,57] Zhang et al[15] and Gong et al[32] also described this phenomenon as the "contact killing" mechanism, where the bacterial membrane would be disturbed by the long fatty alkyl chains of QAS.[15,29,32] Poly (2-tert-butylaminoethyl) methacrylate (PTBAEMA) is a polycationic polymer and has been recognized as a very effective contact biocide with the benefit of less toxicity and no bacterial

resistance.[31,41,58] The charged amino groups of PTBAEMA substituted divalent cations (Ca^{2+}, Mg^{2+}) that cross or bridge the outer membrane of the bacteria, leading to membrane incompetence and disintegration of the cell.[31,41] Dimethyl-amino-dodecyl methacrylate (DMADDM), a branch of QAM, can be copolymerized with DBR[15,29,37] and is used as an antimicrobial agents in dental resins, bonding agents, and glass-ionomer cement.[29] The hydrophilic property of heat-polymerized DMADDM-DBR results in the inhibition of *C. albicans* biofilm, reducing bacterial adhesion or hyphal development on denture surfaces.[29,37] Zhou et al[48] showed that N,N-dimethyl-2-[(2-methylacryloyl)oxy] ethanaminium 5-carboxy-2,4-bis benzoate (DMAEMA-PMDPM) salt had antimicrobial activities against *Streptococci mutans* and *C. albicans* and that the DMAEMA-PMDPM hydrophilic monomer may impart antimicrobial properties to DBRs and soft lining denture materials.[48]

Methacryloyloxy dodecyl pyridinium bromide (MDPB) and methacryloyloxy undecyl pyridinium bromide (MUPB) have been incorporated into DBR.[26,61] The addition of MDPB to dental composite resins reduced bacterial adhesion and plaque accumulation without losing the active constituent,[26] which could be explained by the direct bacterial contact[61] and positive-negative charge interaction mechanisms.[62] 2-methacryloxylethyl dodecyl methyl ammonium bromide (MAE-DB) is known to have antibacterial function,[64] and, when incorporated into DBR (10% wt/vol), it was reported to have powerful bactericidal efficacy against oral bacteria, which may be beneficial in preventing secondary caries on teeth associated with an appliance.[38]

Methallyl phosphate (MAP) is made by adding phosphate anions to PMMA and may improve the antimicrobial activity on DBR by diminishing biofilm formation, as phosphate anions have an important function as a natural salivary defense function in the oral cavity.[44]

Phytochemical or phytomedical components

Essential oils and plant extracts have long been associated with therapeutic properties,[22] and the incorporation of natural organic components into dental materials has been proposed.[13] The cinnamon tree (*Cinnamomum zeylanicum*) possesses favorable analgesic, antiseptic, antispasmodic, astringent, insecticide, and antimicrobial properties.[22] The phytochemical substances from *C. zeylanicum* leaves, such as eugenol, cinnamaldehyde, citral, and geraniol, may play an important role in inhibiting *C. albicans* biofilm formation on DBR surfaces and oral epithelial cells.[22] Additionally, monoterpene molecules from the essential oil provide hydrophobic properties, which permits the deletion of lipophilic structures, inhibiting microbial membrane synthesis, spore germination, and cell respiration.[65] However, the risk of dermatosis (irritation or photosensitivity) is seen as a disadvantage of their use.[22] Hinoki cypress (*Chamaecyparis obtusa*) extract has been used in many household health products, such as soap, toothpaste, and cosmetics because *C. obtusa* essential oil inhibits the development of pathogen microorganisms.[66-68] DBR containing microencapsulated *C. obtusa* essential oil discharged the antimicrobial agent at pH 5.5 and prohibited the growth of the *C. albicans*.[13] Henna powder (*Lawsonia inermis Linn*) is used as a cosmetic, an anti-fever medicine, a local anesthetic, and a treatment for oral ulcers because of its biological hypoglycemic, hepatoprotective, immunostimulatory, anti-inflammatory, antiparasitic, antitrypanosomal, antidermatophytic, antioxidant, contraceptive, tuberculostatic, and anticancerous properties.[42,69] DBR incorporated with henna powder demonstrated antifungal effects against *C. albicans* for 2 weeks and was effective as a denture stomatitis treatment. Although allergic reactions have been reported, henna is generally safe in moderate dosages.[42] Neem trees (*Azadirachta indica*) are native to the subcontinent of India and have been used in traditional remedies because of characteristics paralleling those of henna powder.[30,34] Soluneem (Vittal Mallya Scientific Research Foundation)

is a commercially available neem antimicrobial agent which has been shown to be safe by acute oral and dermal toxicity testing.[30] Auto- and heat-polymerizing DBR materials containing neem extract demonstrated antimicrobial activity against *C. albicans* over a period of 21 days.[30] Another study using neem powder at various concentrations, including 0, 0.5, 1, 1.5, 2, and 2.5 wt%, incorporated into heat-polymerizing DBR showed a substantial reduction of *C. albicans* CFUs from 2061.4 (0%) to 340.8 (2.5%).[34] Tea tree oil (TTO), from a known Australian native plant (*Melaleuca alternifolia*), has been extensively used for antimicrobial purposes.[70] It contains over 48 volatile substances including terpinen-4-ol, which is primarily responsible for the antimicrobial properties.[25] Dalwai et al[25] polymerized heat-polymerizing DBR with TTO in microcapsules and concluded that its antifungal activity was because terpinen-4-ol changed cell membrane properties and compromised the membrane-related functions. Thus, microencapsulation drug delivery technology for TTO was a beneficial approach to medication delivery,[25] although lipophilicity and volatilization were major challenges to the effectiveness of microencapsulated TTO.[25]

Other compounds

1,4-diazabicyclo [2.2.2] octane (DABCO), a colorless solid substance, is a highly nucleophilic amine which is used as a catalyst and reagent in polymerization.[37] The incorporation of DABCO derivatives into DBR materials demonstrated fungicidal action with low cytotoxicity to mammalian cells, while the authors reported that the longevity and sustainability of the material needed to be investigated further.[37] Chitosan is a polycationic biopolymer derived from chitin, and can be found in crustacean shells, insect cuticles, and fungal cell walls.[21,71-74] It is a versatile alkaline hydrophilic polysaccharide material and is biocompatible and nontoxic with adequate permeability, polyelectrolyte action, antimicrobial or anti-inflammatory, and wound healing

effects.[72] Biodegradability is another exceptional property.[21,71] Because of its natural inherent antimicrobial polymer property,[75] chitosan quaternary ammonium salt (CQAS) was investigated by Song et al,[21] who concluded that the interaction between the positively charged amino group of chitosan glucosamine[74] and the electronegative lipid bacterial cell membranes was responsible for antimicrobial activity.[21,71] As a bioactive filler, surface pre-reacted glass-ionomer (S-PRG) produces various ions such as F^{-}, Na^{+}, BO_3^{3-}, Al^{3+}, SiO_3^{2-}, and Sr^{2+}, which promote mineralization on the tooth surface.[47,76] Thus, S-PRG has been used for dental materials such as composite resins, bonding agents, cements, resin sealants, and mouthwashes for its antimicrobial activity against various oral bacteria and for preventing biofilm formation.[76] Due to its antimicrobial effectiveness against cariogenic microorganisms, fluoride has been added to denture surface coating and denture base lining material in an attempt to control dental caries.[8,59,60] Perfluorooctylethyl acrylate (C8F) as a fluoromonomer was added to PMMA, and the increased surface tension resulted in hydrophobic surfaces and a significantly lower degree of *C. albicans* adhesion.[35] Kurata et al[40] demonstrated the antibacterial activity of tri-n-butyl (4-vinylbenzyl) phosphonium chloride (VP). Like chitosan, the mechanism for antibacterial activity of the VP appears to be associated with positive-negative charge interactions between VP cations and the bacterial cell membrane.[40]

CONCLUSIONS

Based on the findings of this systematic review, the following conclusions were drawn:

1. Extensive research has been conducted on improving or developing the antimicrobial effectiveness of DBRs by incorporating various substances.

2. Most of the studies using antimicrobial organic compounds, such as copolymer or acrylic monomer, quaternary ammonium, and phytochemical related materials, exhibited efficacy in reducing the biofilm on DBR surfaces.
3. Several studies also explored natural organic substances such as cinnamon, hinoki cypress tree, henna powder, neem tree extract, and tea tree essential oil, which are known to possess active antimicrobial effects with fewer side effects. However, these materials are limited in their ability to successfully synthesize with DBR materials, and the rapid release of the substance is problematic as it evaporates at room temperature.
4. Considering the negative effects of disinfectants on the environment and uncontrolled antibiotic use contributing to the growth of resistant microbial strains, possible side effects, and the high potential cost to patients, further investigation of innovative techniques to incorporate biodegradable slow release microcapsules or nanocarriers containing natural organic antimicrobial substances able to carry and release the ideal dose into DBRs would improve long-term efficiency.

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TABLES

Table 1. Key search terms and number of articles identified in database systems

Database	Setting	Search terms	Number of articles	Accessed date
Embase	Quick search, no limit	Denture base resin and antibacterial Denture base resin and antifungal Denture base resin and antimicrobial	148 34 157	22/02/2019
Google Scholar	Sort by relevance	Denture base resin and antibacterial Denture base resin and antifungal Denture base resin and antimicrobial	1250 (600) 934 (600) 1260 (600)	26/02/2019
PubMed	Format: summary, sort by most recent	Denture base resin and antibacterial Denture base resin and antifungal Denture base resin and antimicrobial	151 22 38	22/02/2019
Web of Science	Basic search, topic relevance	Denture base resin and antibacterial Denture base resin and antifungal Denture base resin and antimicrobial	50 67 69	25/02/2019
Total			4180 (2536)	

Table 2. Summary of three material groups incorporated as antimicrobial agents

Classification	Type of the incorporated antimicrobial agents		References
Organic	Antimicrobial copolymer or acrylic monomer	2-hydroxyethyl methacrylate (HEMA)/ phosphoric acid 2-hydroxyethyl methacrylate ester (PA2HEME)	Karkosh et al 2018[8]; Yassin et al 2016[39]
		2-methacryloxylethyl dodecyl methyl ammonium bromide (MAE-DB)	Huang et al 2012[38]
		Dimethylaminododecyl methacrylate (DAMDDM)	Chen et al 2017[29]; Zhang et al 2016[15]
		Methacryloyloxy undecyl pyridinium bromide (MUPB)	Regis et al 2012[26]
		Methallyl phosphate (MAP) or phosphate poly (methyl methacrylate)	Raj and Dentino 2011[44]
		Methacrylic acid (MAA)	Gupta et al 2017[33]
		N, N-dimethylaminoethyl methacrylate (DMAEMA)	Mirizadeh et al 2018[28]
		N, N-dimethyl-2-[(2-methylacryloyl)oxy] ethanaminium 5-carboxy-2,4-bis benzoate (DMAEMA-PMDPM)	Zhou et al 2014[48]
		Poly (2-tert-butylaminoethyl) methacrylate (PTBAEMA)	Compagnoni et al 2012[31]; Marra et al 2012[41]
		Quaternary ammonium methacrylates (QAM) /salts compounds (QAS)/ Quaternary ammonium methacryloxy silicate (QAMS)	Gong et al 2012[32]; Hayashi et al 2003[35]; He et al 2013[36]; Pesci-Bardon et al 2006[43]
	Phytochemical or phytomedical components	Cinnamon (*Cinnamomum zeylanicum*)	Oliveira et al 2014[22]
		Hinoki Cypress (*Chamaecyparis obtusa*)	An et al 2018[13]
		Harazi - Yamani henna powder (*Lawsonia inermis Linn*)	Nawasrah et al 2016[42]
		Neem tree extract/powder (*Azadirachta indica*)	Chincholikar et al 2019[30]; Hamid et al 2019[34]
		Tea tree (*Melaleuca alternifolia*)	Dalwai et al 2014[25]
	Other compounds	1,4 diazabiocyclo [2.2.2] octane (DABCO)	Herman et al 2017[37]
		Chitosan quaternary ammonium salt (CQAS)	Song et al 2016[21]
		Fluoroalkyl acrylate monomer-Perfluorooctylethyl acrylate (C8FA)	Hayashi et al 2003[35]
		Surface pre-reacted glass-ionomer (S-PRG) fillers	Tsutsumi et al 2016[47]
		Tri-n-butyl(4-vinylbenzyl) phosphonium chloride (VP)	Kurata et al 2011[40]

FIGURES

Figure 1. Flow diagram representing final number of articles selected.

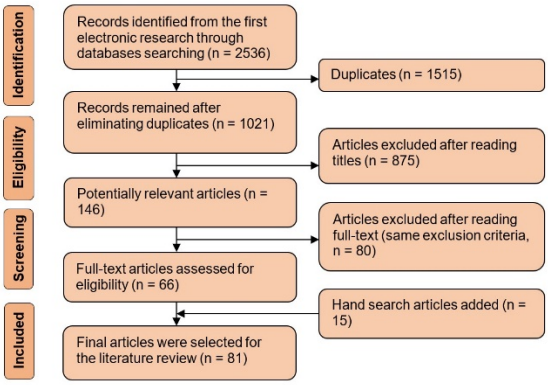
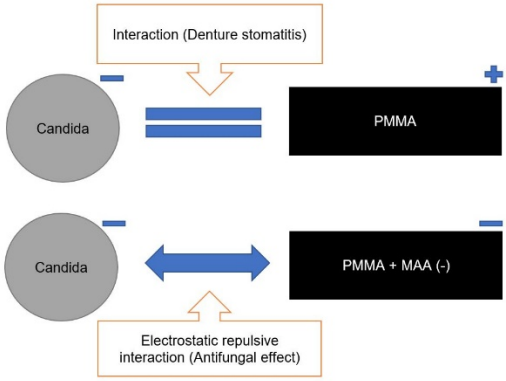


Figure 2. Schematic diagram illustrating process for antifungal activities.



SUPPLEMENTARY TABLES

Supplementary Table 1. Summary of included studies for organic antimicrobial agents

Author	Incorporated antimicrobial materials	Antimicrobial test methods and analyses	Antimicrobial effects results or evaluation	Conclusion or knowledge gaps
An et al 2018[13]	PTMCs containing *Chamaecyparis obtusa* essential oil	OD	At pH 7.4, no release of phytoncide from the PTMCs in the DBR	The antimicrobial agent was released from the PTMCs and inhibition of the growth of the *C. albicans* at pH 5.5 at concentrations were shown
Chen et al 2017[29]	DMADDM	XTT and CFU	Resins containing DMADDM reduced the biofilm at different concentrations	Successful development of the double-decked acrylic resin, effective inhibition of *C. albicans* biofilm with good physical properties
Chincholikar et al 2019[30]	Fluconazole and Soluneem (herbal neem extract)	HPLC and zones of inhibition	Fluconazole exhibited better elution function and antifungal activity against *C. albicans* as compared to control one (herbal neem extract)	Verifying its clinical performance by studying the long-term release of both the materials
Compagnoni et al 2012[31]	PTBAEMA	CFUs	10% PTBAEMA acrylic resins decrease the adhesion of *S. mutans* and *S. aureus,* but no antimicrobial effect against *C. albicans*	N/A
Dalwai et al 2014[25]	Tea tree oil, CG, and fluconazole	Turbidity	CG and tea tree oil inhibited *Candida* up to the 14th day, whereas no antifungal effect of fluconazole after 7th day in the immersion solutions	Tea tree oil used and demonstrated the similar antifungal effects of the CG
Gong et al 2012[32]	QAMS	The percentage distribution of live and dead microbes	QAMS-containing orthodontic acrylic resins exhibited antibacterial and antifungal properties	The retention of antimicrobial activity in dental materials over time
Gupta et al 2017[33]	MAA	CFU using a quadrant streaking method	Addition of MAA to the MMA monomer significantly reduced the adhesion of *S. aureus*	Further investigations on clinical application
Hamid et al 2019[34]	Neem tree powder (*Azadirachta indica*)	Slide counting and direct culture methods, CFU	The addition of neem significantly decreased the *C. albicans*	PMMA acrylic resin containing neem tree powder could be beneficial for the denture stomatitis treatment or prevention. Further studies on the physical tests and various microorganisms
Hayashi et al 2003[35]	C8FA	Counting for the number of adhered *C. albicans* cells under a microscope	Unpolished specimens had a greater the degree *C. albicans* adhesion than that polished samples for both the C8FA and control. The degree of *C. albicans*	The low surface energy of the fluoropolymer had a huge impact on the hydrophobic adhesion of *C albicans* to the new resin (declined adhesion)

			adhesion for C8FA was significantly lower than control	
He et al 2013[36]	Alkyl chain length quaternary ammonium methacrylate monomers (QAM C10-C18)	CFU	Increasing of substituted alkyl chain length of QAM demonstrated the best inhibition effectiveness (Antibacterial activity of copolymer)	The substituted alkyl chain length of QAM led to an influence on antibacterial activity (The longer the alkyl chain, the better the antibacterial activity)
Herman et al 2017[37]	DABCO	XTT and disc diffusion assay	*C. albicans* biofilm formation, and fungal growth was inhibited with the acrylic resin containing 1, 2, or 4 wt% DABCO compounds	Incorporating DABCO derivatives can be used in the denture base materials and exert fungicidal activity with minimal cytotoxicity to mammalian cells
Huang et al 2012[38]	MAE-DB	CFU and real-time qPCR	10% MAE-DB resin suppressed the growth of *S. mutans*	The MAE-DB monomer into resin materials improves its antibacterial properties with at relatively high concentrations
Karkosh et al 2018[39]	PA2HEME, dental varnish layer coating	CFUs	The PA2HEME group showed the lowest number of *C. albicans* against varnish coated groups	The negatively charged PMMA and varnish coated PMMA can be considered to be a therapeutic way for preventing denture stomatitis
Kurata et al 2011[40]	VP, AC, and MA	Evaluation by turbidimetry with CV and CFU	The antibacterial activity of VP copolymer against *S. mutans* was high, while the antibacterial activity of MA and VP copolymer was lower	N/A
Marra et al 2012[41]	PTBAEMA	CFU	Significant antimicrobial activity at 10% and 25% of PTBAEMA against *S. aureus* and *S. mutans* but no significant effect against *C. albicans*	N/A
Mirizadeh et al 2018[28]	DMAEMA	CFU, Agar diffusion test, and FTIR	99% of decreased CFU in *E. coli*, *S. aureus*, and *C. albicans* for 12%-quaternized ammonium modified denture base than control	DBR containing immobilized quaternized ammonium monomer (QAM) demonstrated high antibacterial effectiveness
Nawasrah et al 2016[42]	Harazi - Yamani henna powder (*Lawsonia inermis Linn*)	Culture-based quantitative assay	The variation in the number of live *Candida*, between the control group and group B (1%, 7.5% or 10% concentration of Harazi) was statistically significant	DBR incorporated with Yamani henna powder could be effective in inhibition of *C. albicans* proliferation; further studies on the physical properties
Oliveira et al 2014[22]	Cinnamon (*Cinnamomum zeylanicum*) Blume leaves essential oil	MIC and MFC	*C. zeylanicum* demostrated anti-*Candida* activity, with MIC = 625.0 μg/mL being equivalent to MFC	No adverse clinical signs were observed after intervention with a satisfactory level of safety and tolerability
Pesci-Bardon et al 2006[43]	Quaternary ammonium polymer	CFUs	Resin specimens containing quaternary ammonium presented a bactericidal effect on *E. coli and S. aureus* at 2%, *P. aeruginosa*: at 10% and a fungicidal effect on *C. albicans* at 50%	2% of quaternary ammonium compound concentration displayed an efficient antiseptic property

Raj and Dentino 2011[44]	MAP was synthesized MMA	Human saliva-coated polymer beads and radio-labelled *C. albicans* cells, as compared with that of PMMA	The saliva mediated adhesion of *C. albicans* was reduced with the PMMA containing >=15% phosphate content	Phosphated PMMA polymers can be used as novel DBR preventing denture stomatitis
Regis et al 2012[26]	MUPB	MIC, MFC, MBC and CFU	The incorporation of MUPB effected the adhesion of *C. albicans*	The antimicrobial activity of MUPB incorporated with DBR did not depend on its elution but was shown to be restricted to *C. albicans*
Sawada et al 2008[45]	FAp-TiO_2	ATP	Significant decrease of *C. albicans* adhesion was observed in FAp-TiO_2	DBR containing FAp-TiO_2 prevents the adhesion of *C. albicans* as a new photocatalysts
Sawada et al 2014[46]	FAp-TiO_2	CFU	DBR containing FAp-TiO_2 displayed greater effectiveness in inhibiting *C. albicans* adhesion and in decomposing methylene blue (MB)	DBR containing FAp-TiO_2 can contribute to improve denture hygiene as a proper material
Song et al 2016[21]	Chitosan QAS	Film contact method, CFUs	Antifungal ability and concentration of added chitosan quaternary ammonium salt demonstrated a positive correlation	DBR incorporated with chitosan quaternary ammonium salt can be a new generation oral denture composite material
Tsutsumi et al 2016[47]	Glass ionomer (S-PRG) fillers	XTT	Slight increase of surface roughness of DBR when S-PRG filler incorporated which reduces the adhesion of *C. albicans*	The S-PRG filler can have the potential impact on reducing *C. albican*s adhesion on DBR but the possibility of increasing the surface roughness of DBR
Yassin et al 2016[8]	HEMA and NaF	CLSM	Fluoride had no effectiveness on the colonisation and biofilm growth of any of the microorganisms in monocultures (*C. albicans, L. casei and S. mutans s*pecies), while in mixed above 3 species biofilms, cell densities were reduced approximately ten-fold on the fluoridated material	A fluoride-releasing copolymer inhibiting acidogenic mixed-species biofilms can be used for controlling cariogenic diseases by limiting biofilm growth
Zhang et al 2016[15]	DMADDM	CFU, and XTT	Significant reduction on biomass and metabolic activity when DMADDM incorporated. DMADDM can inhibit the hyphal development of *C. albicans*	DBR containing DMADDM may be considered as a new promising therapeutic approach against *C. albicans* induced disease
Zhou et al 2014[48]	DMAEMA-PMDPM salt	MIC and MBC, time-kill study and MTT	Liquid polymerizable DMAEMA-PMDPM salt display some antimicrobial activity and similar cytotoxicity to common dental resin monomers	Incorporating DMAEMA-PMDPM can have great applications on antimicrobial coatings on DBRs and soft lining materials and other biomedical products

AC, Acrylic acid; ATP, Luminescent adenosine triphosphate; C8FA, Fluoroalkyl acrylate monomer-perfluorooctylethyl acrylate; CG, Chlorhexidine gluconate or digluconate; CFUs, Colony-forming units; CLSM, Confocal laser scanning microscope; CV, Crystal violet; DABCO, 1,4 Diazabiocyclo [2.2.2]

Octane; DBR, Denture base resin; DMADDM, Dimethylaminododecyl methacrylate; DMAEMA, N,N-dimethylaminoethyl methacrylate; DMAEMA-PMDPM, N,N-dimethyl-2-[(2-methylacryloyl)oxy] ethanaminium 5-carboxy-2,4-bis benzoate; FAp-TiO_2, Fluoridated apatite-coated titanium dioxide; FTIR, Fourier transform infrared spectroscopy; HEMA, 2-hydroxyethyl methacrylate; HPLC, High-performance liquid chromatography; MA, Methacryloyloxyethyl trimethyl ammonium chloride; MAA, Methacrylic acid; MAE-DB, 2-methacryloxylethyl dodecyl methyl ammonium bromide; MAP, Methallyl phosphate; MBC, Minimum bactericidal concentration; MFC, Minimum fungicidal concentration; MIC, Minimum inhibitory concentration; MMA, Methyl methacrylate; MTT, 3-(4,5- Dimethylthiazol- 2- il)- 2,5- diphenyltetrazolium bromide; NaF; Sodium fluoride; OD; Optical density; PA2HEME, Phosphoric acid 2-hydroxyethyl methacrylate ester; pH Potential hydrogen; PMMA, Polymethyl methacrylate; PTBAEMA, 2-tert-butylaminoethyl methacrylate; PTMCs, Phytoncide microcapsules; QAMDB, quaternized ammonium modified denture base; Quaternary ammonium methacryloxy silicate; QAS, Quaternary ammonium salt; qPCR, Quantitative polymerase chain reaction; S-PRG, Surface pre-reacted glass-ionomer; VP, Tri-n-butyl(4-vinylbenzyl)phosphonium chloride; XTT, Tetrazolium salt 2,3-bis (2-methoxy-4-nitro-5-sulfophenyl)-5-[(phenylamino) carbonyl]-2H-tetrazolium hydroxide.